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Centers Needed to Study Women's Environmental Health

The view of women as primarily fecund beings goes back to prehistory, where it is expressed in the well-known series of Venuses—stone figures of women with enlarged breasts, who are often represented as pregnant. Although the Venus figures date from the late Paleolithic era, this view of women did not change much in the next 20,000 years. With the approaching millennium, however, the field of health research has begun to consider women apart from their children or prospective progeny. Reflecting this shift in viewpoint, funds for research on the environmental health of women have now become available. However, no coordinated program has been launched on the scale of the newly established Centers for Children's Environmental Health and Disease Prevention Research (1). Should women, like children, be the focus of a concerted research effort?

The new program for children developed from the persuasive argument, first made in the 1993 National Academy of Sciences report on *Pesticides in the Diet of Infants and Children* (2), that there are salient age-related differences between children and adults. The report marshaled the evidence that children are more vulnerable to the effects of environmental agents. Because of physiologic reasons, as well as age-related behaviors, children's exposures tend to be higher and may also be more toxic. Children tend to metabolize compounds faster but detoxify more slowly. Differences in body size and composition also affect levels of toxicity. In addition, there are critical windows of time in children's lives when vulnerability to the adverse effects of exposure is increased, most notably during dynamic periods of growth and development.

What about women? The whole field of women's health is premised on the existence of gender differences in disease occurrence, severity, and outcome (3), but how important are they to understanding the spectrum of effects of environmental agents or the impact of environmental factors on women's health? Because space does not allow for an exhaustive response, the reader is referred to the recent Institute of Medicine (IOM) report on *Gender Differences in Susceptibility to Environmental Factors ...* (4) for a more complete discussion. A few points are presented here to indicate the scope and significance of these differences.

In the United States, women typically spend more time in their homes and neighborhood environments than men do, potentially increasing their exposures to such toxic agents as indoor and outdoor pesticides, as well as pollution and ultraviolet radiation. Contextual effects of neighborhood environments, which are emerging as an important consideration for public health research (5), are likely to have a greater impact on women than on men.

Women have more body fat than men and may store more fat-soluble toxic material, even when exposed to the same amount as men. Plasma dioxin concentrations have recently been found to be elevated in women as compared to men exposed at the same level, even after adjustment for a number of factors such as body mass index (6). Landi et al. (6) suggest that body fat, hormones, and metabolic differences are possible explanations.



Certain stages in a woman's life—like periods of growth and development in children—may influence susceptibility to environmental agents, principally through change in the concentrations of certain hormones. Puberty, the reproductive years, perimenopause, and postmenopause are all points where susceptibility to exposure may be different because of an altered hor-

monal milieu. The importance of cyclic hormone levels has led to the suggestion that a lifespan approach should be taken in studying women (although this suggestion is more honored in the breach).

Hormones are also responsible for the greater immunoreactivity of women (7), a phenomenon that is largely estrogen driven and that contributes to the widely recognized female excess of autoimmune disorders. There is increasing interest in the role of the environment in the etiology of these diseases.

Female hormones have been proposed to enhance susceptibility to toxins by deregulating growth and differentiation via receptor binding (8). Because metabolizing genes are not sex linked, there should be no gender difference in frequency, although there could be gender differences in the basal expression of genetic polymorphisms. Hormones could interact to affect inducibility of detoxifying enzymes. Some argue that neither expression nor induction of metabolizing enzymes is likely to account for observed gender differences in adverse effects of exposure, but rather that these gender differences are caused by an as yet unidentified difference in sensitivity to toxic compounds (9). Clearly, it is extremely important to find the reasons for gender variation in susceptibility.

Research on women's health is already taking place in the absence of a centers program. (Of course this was also true in the case of children.) Perhaps the best known research to date has focused on pesticides, polychlorinated biphenyls, and breast cancer. Fifteen papers have now been published on this topic [Helzlsouer et al. (10) provides a summary]; the results, although mixed, have been largely negative. However, many community-based women's groups believe the environment contributes to the risk of breast cancer, so it is possible—perhaps likely—that new environmental hypotheses will emerge.

Another example of ongoing work is the studies of environmental influences on certain gynecologic disorders with high levels of morbidity. Following a provocative study in monkeys who developed endometriosis after exposure to dioxin (11), effects on endometriosis are being investigated in women from the area around Seveso, Italy, where dioxin levels are high due to an industrial accident. Because dioxin is known to have hormonal activity, results from this research will contribute data to the endocrine-disruptor initiative.

There is also active women's health research in toxicology and basic science—areas such as molecular toxicology and receptor-based biology; unfortunately, no real mechanism exists for ensuring

an exchange of results and ideas with scientists doing research in humans.

In spite of the ongoing activity, the IOM report's (4) review of federally funded work related to women concluded that there were too few studies of environmental exposures and women's health and that even data on the nature of women's exposures were lacking. Neuroendocrine and immune disorders in women were identified as priorities for future work. Postmenopausal women, elderly women, and the roles of race, ethnicity, and culture were all cited in the IOM report as deserving attention.

Given the range of environmental issues affecting women, it seems unlikely that an adequate picture can be obtained through scattered studies. It is improbable that a meaningful exchange with scientists in different disciplines will take place under current circumstances. Thus, it seems nearly impossible that the evidence gathered can be translated effectively into new clinical guidelines or preventive interventions. To promote the performance of research that will have maximum impact on knowledge, prevention, and treatment of women's environmental health, it will take an integrated program of interdisciplinary centers with a clear, prioritized agenda.

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REFERENCES AND NOTES

1. Carroquino MJ, Galson SK, Licht J, Amler RW, Perera FP, Claxton LD, Landrigan PJ. The U.S. EPA Conference on Preventable Causes of Cancer in Children: a research agenda. *Environ Health Perspect* 106(suppl 3):867-873 (1998).
2. National Academy of Sciences. *Pesticides in the Diet of Infants and Children*. Washington, DC:National Academy Press, 1993.
3. Chesney MA, Ozer EM. Women and health: in search of a paradigm. *Women's Health: Res Gender Behav Policy* 1:3-26 (1995).
4. Institute of Medicine. *Gender Differences in Susceptibility to Environmental Factors: A Priority Assessment*. Washington, DC:National Academy Press, 1998.
5. Malmstrom M, Sundquist J, Johansson S-E. Neighborhood environment and self-reported health status: a multilevel analysis. *Am J Public Health* 89:1181-1186 (1999).
6. Landi MT, Consonni D, Patterson DC Jr, Needham LL, Lucier G, Brambilla P, Cazzaniga MA, Mocarrelli P, Pesatori AC, Bertazzi PA, et al. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin plasma levels in Seveso 20 years after the accident. *Environ Health Perspect* 106:273-277 (1998).
7. Cannon JG, St. Pierre GA. Gender differences in host defense mechanisms. *J Psychiat Res* 31:99-113 (1997).
8. Perera FP. Environment and cancer: who are susceptible? *Science* 278:1068-1073 (1997).
9. Lasley BL. Gender differences in metabolism and susceptibility to environmental exposures. In: Institute of Medicine. *Gender Differences in Susceptibility to Environmental Factors: A Priority Assessment*. Washington, DC:National Academy Press, 1998:53-58.
10. Helzlsouer KJ, Alberg AJ, Huang H-Y, Hoffman SC, Strickland PT, Brock JW, Burse VW, Needham LL, Bell DA, Lavigne JA, et al. Serum concentrations of organochlorine compounds and the subsequent development of breast cancer. *Cancer Epidemiol Biomark Prev* 8:525-532 (1999).
11. Rier SE, Martin DC, Bowman RE, Dmowski WP, Becker JL. Endometriosis in rhesus monkeys (*Macaca mulatta*) following chronic exposure to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. *Fundam Appl Toxicol* 21:433-441 (1993).